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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
11/10/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/561,022	SAITO ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,12-15,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,12-15,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/10/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 8/10/09 has been entered in full. Claims 1, 4 and 5-7 are amended. Claims 10, 11 and 16-21 are canceled (claims 8 and 9 were canceled previously). New claims 22 and 23 are added.

In view of Applicants' cancellation of all of the claims of Group II (claims 10, 11 and 16-21), the restriction requirement between Group I and II is currently moot, but will be reinstated if claims to Group II are re-introduced in subsequent claim amendments.

Claims 1-7, 12-15, 22 and 23 are under consideration in the instant application.

Information Disclosure Statement

The Information Disclosure Statement of 8/10/09 has been considered.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (2/20/09).

Applicants' response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (2/20/09) has been considered and is found persuasive. Applicants' 8/10/09 response included Replacement Sheets for Figure 1-4 and 6-9 that include the relevant sequence identifiers for the disclosed sequences. Therefore, the requirements set forth in the Office Action of 3/2/09 are *withdrawn*.

The rejection of claims 6 and 7 under 35 U.S.C § 112, second paragraph, at pg 2-3 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is *withdrawn* in view of Applicants' amendments to the claims.

The rejection of claims 1-7 and 12-15 under 35 U.S.C. § 112, first paragraph at pg 3-11 for failing to provide enablement for the claims is *withdrawn* in view of Applicants' amendments to the claims, and further in view of Applicants' persuasive arguments at page 6-7 of the response, and further in view of the teachings of Wells et al, 2009 (International Journal of Medical Microbiology. 8 pages). In a review of innate

signaling and immunity in the intestine, Wells et al summarize evidence supporting a role for at least TLR2, 3, 4, 5, 6 and 9 in activation of intestinal innate immunity.

The rejection of claims 1-7 and 12-15 under 35 U.S.C. § 112, first paragraph at pg 11-14 for failing to comply with the written description requirement is *withdrawn* in view of Applicants' amendments to the claims.

The rejection of claims 6 and 7 under 35 U.S.C. 103(a) at pg 22-24 as being unpatentable over Akira et al, WO 02/06482, as applied to claim 5, and further in view of Kitazawa et al (2003) is *withdrawn* in view of Applicants' amendments to claim 6 that specify more precisely the relationship of the additional limitations of claim 6 to the method of parent claim 5. However, please see the new rejection of claims 6 and 7 under 35 U.S.C. 103(a) as being unpatentable over Akira et al, WO 02/06482, as applied to claim 5, and further in view of Kitazawa et al (2003) that is necessitated by Applicants' amendments to the claims.

The rejection of claims 6 and 7 under 35 U.S.C. 103(a) at pg 24-26 as being unpatentable over Lipford et al, WO 2004/026888, as applied to claim 5, and further in view of Kitazawa et al (2003) is *withdrawn* in view of Applicants' amendments to claim 6 that specify more precisely the relationship of the additional limitations of claim 6 to the method of parent claim 5. However, please see the new rejection of claims 6 and 7 under 35 U.S.C. 103(a) as being unpatentable over Lipford et al, WO 2004/026888, as applied to claim 5, and further in view of Kitazawa et al (2003) that is necessitated by Applicants' amendments to the claims.

Maintained Objections and/or Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 12, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Akira et al, WO 02/06482 (published January 24, 2002; reference F2 on

the 7/27/06 IDS (no translation provided). The '482 publication of Akira et al is in Japanese; however, this reference is a publication of PCT/JP01/04731 and therefore an identical disclosure in English can be found in Akira et al, U.S. Patent Application Publication 20030124655 (reference U1 on the 7/25/05 IDS), which is a 371 of the same PCT. Thus, the paragraphs referenced below refer to the '655 publication. This rejection was previously set forth at page 14-19 of the 2/20/09 Office Action.

Applicants have amended independent claim 1 (from which all other claims depend) to limit the cell to an "isolated" cell expressing a "naturally-occurring mammalian" intestinal tract tissue-expressed Toll-like receptor. In the rejection set forth previously, the cells were cultured cells (see page 16 of the 2/20/09 Office Action), and thus encompassed by the term "isolated". Furthermore, the cells expressed human-derived TLR9 (see page 16 of the 2/20/09 Office Action), and thus are encompassed by a "cell expressing a naturally-occurring mammalian intestinal tract tissue-expressed Toll-like receptor". Therefore, the rejection set forth previously is maintained for the reasons of record (at page 14-19 of the 2/20/09 Office Action).

Applicants' arguments (8/10/09; pg 8-11) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants argue that "crucial claim limitations" including the claim limitation that recites "for assessing whether a test sample activates the intestinal tract immune system" and the "judgment" step in the concluding statement (as recited in claim 1 and encompassed by the dependent claims) "have, improperly, not been given patentable weight" (pg 8). Applicants quote several section from MPEP 2111.02 and argue that a "preamble's statement of intended use must be given patentable weight when, as in this case, it gives "life, meaning and utility" to the claim, and when it helps to distinguish from the prior art" (pg 10). Applicants argue that the Metabolite Labs case cited in MPEP 2111.02 "provides important insight into the proper interpretation of both the preamble" of claim 1 "as well as the "judgment" step". Applicants argue that the preamble and "correlating" step from the Metabolite Labs case were treated as critical claim limitations to distinguish the invention from the prior art. Applicants further argue that "there is no basis in law or logic for emphasizing" the claim limitation of the

preamble "for purposes of enablement but then ignoring it for purposes of distinguishing from the prior art". Applicants further argue that Akira et al do not each "that activation of TLRs in a cell-based assay is associated with the activation of the intestinal immune system" and therefore Akira et al do not provide a method required by Applicants' claims.

Applicants' arguments have been fully considered but are not found persuasive. MPEP 2111.02 begins with the statement that the "determination of whether a preamble limits a claim is made on a case-by-case basis in light of the facts in each case; there is no litmus test defining when a preamble limits the scope of a claim" (citing *Catalina Mktg. Int 'l v. Coolsavings.com, Inc* (2002). Thus, the decision in the "Metabolite Labs case" cannot be applied to the instant case as a "litmus test defining when a preamble limits the scope of claim". The fact patterns of the "Metabolite Labs case" cited by Applicants and of the instant rejection are significantly different, and the court decisions are not binding with regard to the instant rejections. The "correlating" step presented in the claims considered in the "Metabolite Labs step" was an active method step that was required to be performed as part of method steps of the claim. In contrast, in the instant claims, what Applicants characterize as a "judgment step" is not a method step, but instead is a "wherein" clause that presents a contingency (a possible conclusion). If the activity of the Toll-like receptor (TLR) is increased as compared to a control cell (not contacted with the test sample), then the test sample is "judged" to be activating the intestinal tract immune system. The "judgment" is a purely mental determination that relates only to the intended use and is therefore inherently met by any test sample that increases the activity of the TLR as compared to a control cell. In other words, this "judgment" does not result in any manipulative difference that patentably distinguishes the instant screening method from prior art screening methods wherein test samples that activate a TLR are identified. Every sample identified as activating a TLR receptor in a prior art method would also be "judged" to be activating the intestinal tract immune system by the instant method. Thus, the rejection of the claims under 102(b) as being anticipated by Akira et al does not require that Akira et al teach "that activation of TLRs in a cell-based assay is associated with the activation of the intestinal immune system"

because the concluding statement does not result in any manipulative difference that patentably distinguishes the instant screening method from prior art screening methods wherein test samples that activate a TLR are identified.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5 and 12-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Lipford et al, WO 2004/026888 (published 1 April 2004, filed 19 September 2003 and claiming priority to 19 September 2002). This rejection was previously set forth at page 19-22 of the 2/20/09 Office Action.

Applicants have amended independent claim 1 (from which all other claims depend) to limit the cell to an "isolated" cell expressing a "naturally-occurring mammalian" intestinal tract tissue-expressed Toll-like receptor. The screening method described in the rejection set forth previously includes use of a "cell line" (pg 36, line 30 of Lipford et al), which are cells encompassed by the term "isolated". Furthermore, the cells expressed various naturally-occurring mammalian TLR9, for example swine TLR9 (see page 22 of the 2/20/09 Office Action), and thus are encompassed by a "cell expressing a naturally-occurring mammalian intestinal tract tissue-expressed Toll-like receptor". Therefore, the rejection set forth previously is maintained for the reasons of record (at page 19-22 of the 2/20/09 Office Action).

Applicants' arguments (8/10/09; pg 11-12) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants argue teach "that activation of TLRs in a cell-based assay is associated with the activation of the intestinal immune system" and therefore Akira et al do not provide a method required by Applicants' claims.

Applicants' arguments have been fully considered but are not found persuasive. As set forth previously and maintained herein, the "judgment" recited in the claims is a purely mental determination that relates only to the intended use and is therefore inherently met by any test sample that increases the activity of the TLR as compared to a control cell. In other words, this "judgment" does not result in any manipulative difference that patentably distinguishes the instant screening method from prior art screening methods wherein test samples that activate a TLR are identified. Every sample identified as activating a TLR receptor in a prior art method would also be "judged" to be activating the intestinal tract immune system by the instant method. Thus, the rejection of the claims under 102(b) as being anticipated by Lipford et al does not require that Lipford et al teach "that activation of TLRs in a cell-based assay is associated with the activation of the intestinal immune system" because the concluding statement does not result in any manipulative difference that patentably distinguishes the instant screening method from prior art screening methods wherein test samples that activate a TLR are identified.

New rejections necessitated by Applicants' amendment

Claim Rejections - 35 USC § 112, 1st paragraph, new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claim contains new matter.

New claim 23 depends from claim 6 and limits the carrier to one that "is acceptable for human consumption". Thus, new claim distinguishes dietarily acceptable carriers that are acceptable for human consumption from dietarily acceptable carrier that are not acceptable for human consumption. Applicants' 8/10/09 response indicates that "[s]upport for the claim amendments can be found in the specification as originally filed". However, the examiner has reviewed the entire specification as originally filed

and cannot find such support for a distinction between dietarily acceptable carriers that are and are not acceptable for human consumption. Such a distinction would divide said carriers in two separate genera based on acceptability for human consumption or lack thereof (e.g., being acceptable only for consumption by a non-human animal). The specification at ¶[0091] (published application) provides examples of dietarily acceptable carriers including "stabilizing agents, preservatives, coloring agents and flavoring agents" but does not distinguish those that are acceptable for human consumption from those that are not. Dietarily acceptable carriers are referenced in ¶[0038] as being part of the claimed method but are not further distinguished. Likewise, the original claims including dietarily acceptable carriers as part of the claimed methods but did not further distinguish said carriers. Thus, while the specification as originally filed provides examples of dietarily acceptable carriers it does not provide a distinction between those that are acceptable for human consumption and those that are not. Nowhere does the specification as originally filed describe the specifically claimed genus encompassing a "carrier that is acceptable for human consumption" of new claim 23. Therefore, the specification as originally filed lacks support for new claim 23.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 7, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akira et al, WO 02/06482 (published January 24, 2002; reference F2 on the 7/27/06 IDS; in light of the translation provided by U.S. Patent Application Publication 20030124655; cited previously) as applied to claim 5 above, and further in view of Kitazawa et al (2003. International Journal of Food Microbiology. 85(1-2):11-21; published 15 August 2003 but available one 16 November 2002; 17 pages as printed; cited previously).

Claim 6 depends from claim 5. In claim 6, the recitation of “for producing a food composition that activates the intestinal tract immune system” in the preamble of the claim is interpreted as an intended use and bears no accorded patentable weight to distinguish the claimed method over one from the prior art. As amended, claim 6 additionally recites a "comprising the method steps of claim 5, and then mixing one or more microorganisms selected in part (b) of claim 5 with a dietarily acceptable carrier". As with parent claim 5, the limitation of "microorganisms assessed to activate the intestinal tract immune system" is met by any microorganisms with an extract that activates the Toll-like receptor when practicing the method steps of the claim.

Claim 7 depends from claim 6, and limits the microorganism to a lactic acid bacterium.

Claims 22 and 23 each depends from claim 6, and encompass a dietarily acceptable carrier that is a dairy product acceptable for human consumption (e.g. yogurt).

As described previously and maintained above, Akira et al teach all of the limitations of claim 5. As noted therein, Akira et al teach that bacterial DNA having an unmethylated CpG sequence can be used in the screening methods for agonists (¶ 54, last sentence). Akira et al do not teach the additional step of claim 6 wherein a microorganism assessed to activate is mixed with a dietarily acceptable carrier, or the additional limitations that the microorganism is a lactic acid bacterium (claim 7) or that the carrier is a dairy product (claim 22) or acceptable for human consumption (claim 23).

Kitazawa et al teach (see Title and Abstract) that an immunostimulatory oligonucleotide with a CpG-like motif (sOL-OB7) exists in the yogurt-producing lactic acid bacterium *Lactobacillus delbrueckii ssp. bulgaricus* (also referred to as *L. bulgaricus*). The art further teaches that said sOL-LB7 immunostimulatory oligonucleotide inherently has the ability to activate cells recombinantly expressing TLR9. Specifically, Shimosato et al (2004) teach "OLLB-7 which is immunostimulatory ODN containing a CpG motif from L. bulgaricus was also injected by CHOK-1^{sTRL9trans} cells (Fig. 1D)" (see page 380 and Figure 1 of Shimosato et al, 2004. Animal Science

Journal, 75: 377-382; cited here to provide evidence of an inherent characteristic of the sOL-LB7 oligonucleotide taught by Kitazawa). Kitazawa et al further teach that "[t]his study demonstrated that *L. bulgaricus* NIAI B6 was a good candidate of a starter culture for the production of new functional foods" (see Abstract) and "*L. bulgaricus* and its metabolites have been reported to exert a wide variety of immunostimulation ... [t]hese findings together with *L. bulgaricus* containing immunostimulatory oligonucleotides OL-LB7 are useful in the production of new special foods, Namely "Bio-Defense Foods" with contribution to the enhancement of the innate and adaptive immunity" (pg 12). Kitazawa et al further teach the skilled artisan "to expect that sOL-LB7 activates the immune cells through its binding to TLR9 and the activation of possible signaling pathways, like CpG oligonucleotides, although it must be elucidated" (pg 12).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to perform the screening method of claim 5 as taught by Akira et al (with bacterial DNA having an unmethylated CpG sequence and a cell expressing a TLR9 receptor), but to substitute an extract (OL-LB7 CpG DNA) from the microorganism (*L. bulgaricus*) taught by Kitazawa et al for the extract (CpG DNA) from the microorganism (bacteria in general) taught by Akira et al, and to further select *L. bulgaricus* as an organism that is assessed as activating the TLR9 receptor, and to further use *L. bulgaricus* to produce yogurt as taught by Kitazawa, thus mixing said microorganism with a dietarily acceptable carrier that is a dairy product acceptable for human consumption. The person of ordinary skill in the art would be motivated to do so because Kitazawa specifically suggests testing to determine if OL-LB7 sequence taught by Kitazawa et al is one of the TLR9 activating CpG sequences taught by Akira et al. Such screening would inherently find that the OLLB-7 CpG DNA from *L. bulgaricus* activates the TLR9 receptor as expressed in a cell, resulting in selecting *L. bulgaricus* as a microorganism that is assessed to activate the TLR9 receptor. As set forth previously for parent claim 5, any microorganism with an extract that activates a Toll-like receptor is inherently assessed to be a microorganism that "activates the intestinal tract immune system". The skilled artisan would further be motivated to produce yogurt using said microorganism in order to produce a food that would contribute to the

enhancement of the innate and adaptive immunity, as taught by Kitazawa et al. Furthermore, a person of ordinary skill in the art would have a reasonable expectation of success in modifying the method Akira et al in view of Kitazawa et al because such modification would merely require applying the specific bacteria containing a CpG motif taught by Kitazawa et al to the general method taught by Akira et al, and further producing yogurt using the bacteria as taught by Kitazawa et al.

Applicants' arguments (8/10/09; pg 12-13) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants argue that the claims have been amended herein "to eliminate any amibiguity that may have contributed to the interpretation of the claims upon which this obviousness rejection has been made" and "new claims have been added to which this combination of references would clearly not be applicable" (pg 13). Applicants argue that the combination of references "could only have been arrived at through the use of impermissible hindsight reconstruction of the prior art", which cannot be used to support a § 103 rejection (citing *In re Sponnable* (1969). Applicants argue combining the prior art requires an apparent reason to combine the known elements in the fashion claimed (citing *KSR International Co. v. Teleflex Inc* (2007)), and in the instant case there is no reason to modify the cited references to arrive at the current invention. Applicants argue that the claims are not obvious ""merely by demonstrating that each of its elements was, independently, known in the (purported) prior art"". Applicants argue that the cited references do not provide a method for identifying microorganisms that stimulate intestinal immune response, and without such knowledge there is no reasons to use the selected organism in preparation of a composition as claimed.

Applicants' arguments have been fully considered but are not found persuasive. As noted above, the rejection of claims 6 and 7 under 35 U.S.C. 103(a) as being unpatentable over Akira et al in view of Kitazawa et al set forth previously has been withdrawn in view of Applicants' amendments to the claims that specify more precisely the relationship of the additional limitations of claim 6 to the method of parent claim 5.

Furthermore, a new rejection of amended claims 6 and 7 and new claims 22 and 23 under 35 U.S.C. 103(a) as being unpatentable over Akira et al in view of Kitazawa et al has been set forth above. In response to Applicants' argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicants' disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In response to Applicants' argument that there is no suggestion to combine the references, the rejection set forth does set forth such suggestion; specifically that Kitazawa et al suggest testing the ability of sOL-LB7 to activate TLR9, thus providing a motivation to combine the teachings of Kitazawa et al with the screening method taught by Akira et al. Furthermore, as with parent claim 5, the limitation of "microorganisms assessed to activate the intestinal tract immune system" is met by any microorganism with an extract that activates the Toll-like receptor when practicing the method steps of the claim.

Claims 6, 7, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipford et al, WO 2004/026888 (published 1 April 2004, filed 19 September 2003 and claiming priority to 19 September 2002; cited previously) as applied to claim 5 above, and further in view of Kitazawa et al (2003. International Journal of Food Microbiology. 85(1-2):11-21; published 15 August 2003 but available one 16 November 2002; 17 pages as printed; cited previously).

Claims 6, 7, 22 and 23 are interpreted as described above.

As described previously and maintained above, Lipford et al teach all of the limitations of claim 5. Lipford et al further teach that the candidate ligand to be tested can be CpG DNA (pg 5, line 11), which is an extract (nucleic acid) from a microorganism (bacterial). Lipford et al do not teach the additional step of claim 6 wherein a microorganism assessed to activate is mixed with a dietarily acceptable

carrier that is a dairy product. Lipford et al do not teach the additional step of claim 6 wherein a microorganism assessed to activate is mixed with a dietarily acceptable carrier, or the additional limitations that the microorganism is a lactic acid bacterium (claim 7) or that the carrier is a dairy product (claim 22) or acceptable for human consumption (claim 23).

Kitazawa et al teach (see Title and Abstract) that an immunostimulatory oligonucleotide with a CpG-like motif (sOL-OB7) exists in the yogurt-producing lactic acid bacterium *Lactobacillus delbrueckii ssp. bulgaricus* (also referred to as *L. bulgaricus*). The art further teaches that said sOL-LB7 immunostimulatory oligonucleotide inherently has the ability to activate cells recombinantly expressing TLR9. Specifically, Shimosato et al (2004) teach "OLLB-7 which is immunostimulatory ODN containing a CpG motif from L. bulgaricus was also injected by CHOK-1^{sTRL9trans} cells (Fig. 1D)" (see page 380 and Figure 1 of Shimosato et al, 2004. Animal Science Journal, 75: 377-382; cited here to provide evidence of an inherent characteristic of the sOL-LB7 oligonucleotide taught by Kitazawa). Kitazawa et al further teach that "[t]his study demonstrated that *L. bulgaricus* NIAI B6 was a good candidate of a starter culture for the production of new functional foods" (see Abstract) and "*L. bulgaricus* and its metabolites have been reported to exert a wide variety of immunostimulation ... [t]hese findings together with *L. bulgaricus* containing immunostimulatory oligonucleotides OL-LB7 are useful in the production of new special foods, Namely "Bio-Defense Foods" with contribution to the enhancement of the innate and adaptive immunity" (pg 12). Kitazawa et al further teach the skilled artisan "to expect that sOL-LB7 activates the immune cells through its binding to TLR9 and the activation of possible signaling pathways, like CpG oligonucleotides, although it must be elucidated" (pg 12).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to perform the screening method of claim 5 as taught by Lipford et al (with bacterial DNA having an unmethylated CpG sequence and a cell expressing a TLR9 receptor), but to substitute an extract (OLLB-7 CpG DNA) from the microorganism (*L. bulgaricus*) taught by Kitazawa et al for the extract (CpG DNA) from the microorganism (bacteria in general) taught by Lipford et al, and to further select *L.*

bulgaricus as an organism that is assessed as activating the TLR9 receptor, and to further use *L. bulgaricus* to produce yogurt as taught by Kitazawa, thus mixing said microorganism with a dietarily acceptable carrier that is a dairy product acceptable for human consumption. The person of ordinary skill in the art would be motivated to do so because Kitazawa specifically suggests testing to determine if OL-LB7 sequence taught by Kitazawa et al is one of the TLR9 activating CpG sequences taught by Lipford et al. Such screening would inherently find that the OLLB-7 CpG DNA from *L. bulgaricus* activates the TLR9 receptor as expressed in a cell, resulting in selecting *L. bulgaricus* as a microorganism that is assessed to activate the TLR9 receptor. As set forth previously for parent claim 5, any microorganism with an extract that activates a Toll-like receptor is inherently assessed to be a microorganism that "activates the intestinal tract immune system". The skilled artisan would further be motivated to produce yogurt using said microorganism in order to produce a food that would contribute to the enhancement of the innate and adaptive immunity, as taught by Kitazawa et al. Furthermore, a person of ordinary skill in the art would have a reasonable expectation of success in modifying the method Lipford et al in view of Kitazawa et al because such modification would merely require applying the specific bacteria containing a CpG motif taught by Kitazawa et al to the general method taught by Lipford et al, and further producing yogurt using the bacteria as taught by Kitazawa et al.

Applicants' arguments (8/10/09; pg 13-14) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants argue that the claims have been amended and that the cited references do not provide a method for identifying microorganisms that stimulate intestinal immune response, and without such knowledge there is no reasons to use the selected organism in preparation of a composition as claimed.

Applicants' arguments have been fully considered but are not found persuasive. As noted above, the rejection of claims 6 and 7 under 35 U.S.C. 103(a) as being unpatentable over Lipford et al in view of Kitazawa et al set forth previously has been withdrawn in view of Applicants' amendments to the claims that specify more precisely

the relationship of the additional limitations of claim 6 to the method of parent claim 5. Furthermore, a new rejection of amended claims 6 and 7 and new claims 22 and 23 under 35 U.S.C. 103(a) as being unpatentable over Lipford et al in view of Kitazawa et al has been set forth above. In response to Applicants' argument that there is no suggestion to combine the references, the rejection set forth does set forth such suggestion; specifically that Kitazawa et al suggest testing the ability of sOL-LB7 to activate TLR9, thus providing a motivation to combine the teachings of Kitazawa et al with the screening method taught by Lipford et al. Furthermore, as with parent claim 5, the limitation of "microorganisms assessed to activate the intestinal tract immune system" is met by any microorganism with an extract that activates the Toll-like receptor when practicing the method steps of the claim.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Bridget E Bunner/
Primary Examiner, Art Unit 1647